THE MERCK INDEX

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CHEMICALS, DRUGS, AND BIOLOGICALS

TWELFTH EDITION

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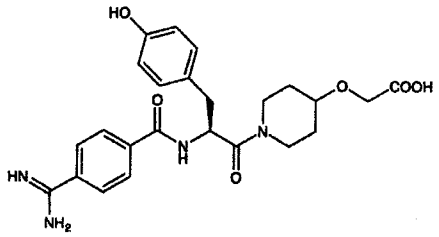
Propionate potassium, $C_{40}H_{65}KO_{13}$, *RS-11988, Cattlyst.* mp 190-192°.

THERAP CAT (VET): Growth promotant.

5362. Lamifiban. *(S)-[[1-[2-[[4-(Aminoiminomethyl)-benzoyl]amino]-3-(4-hydroxyphenyl)-1-oxopropyl]-4-piperidinyl]oxy]acetic acid;* [[1-[*N*-(*p*-amidinobenzoyl)-L-tyrosyl]-4-piperidinyl]oxy]acetic acid; Ro 44-9883. $C_{24}H_{28}N_4O_6$; mol wt 468.51. C 61.53%, H 6.02%, N 11.96%, O 20.49%. Specific nonpeptide platelet fibrinogen receptor (GPIIb/IIIa) antagonist. Prepn: L. Alig *et al.*, **Eur. pat. Appl. 505,868;** *eidem,* **U.S. pat. 5,378,712** (1992, 1995 both to Hoffmann-La Roche); L. Alig *et al., J. Med. Chem.* **35,** 4393 (1992). Pharmacology: J.-P. Carteaux *et al., Thromb. Haemostasis* **70,** 817 (1993); Y. Takiguchi *et al., ibid.* **73,** 683 (1995).



Crystals (zwitterionic form) from water, mp above 200° (dec). $[\alpha]_D^{20}$ +29.8° (c = 0.86 in 1*N* HCl).

Trifluoroacetate salt, $C_{24}H_{28}N_4O_6.C_2HF_3O_2$, mp 125-130° (dec). LD_{50} i.v. in mice: 250 mg/kg (Alig, 1995).

THERAP CAT: Antithrombotic.

5363. Laminaran. Laminarin. A polysaccharide found in brown seaweed and occurring principally in the *Laminaria* spp. Linear polymer composed of β-(1→3)-linked glucose residues; may contain small amounts of β-(1→6) linkages as interresidue linkages or as branch points and 2-3% D-mannitol as end groups. Two forms of laminaran are recognized; they are referred to as soluble and insoluble laminaran: Percival, Ross, *J. Chem. Soc.* **1951,** 720. Structure: Peat *et al., ibid.* **1958,** 724, 729; **1960,** 175; Goldstein *et al., Chem. & Ind. (London)* **1959,** 124; Annan *et al., ibid.* **1962,** 984; Annan *et al., J. Chem. Soc.* **1965,** 885; Maeda, Nisizawa, *Carbohyd. Res.* **7,** 97 (1968). Structure of soluble laminaran from *Eisenia bicyclis:* T. Usui *et al., Agr. Biol. Chem.* **43,** 603 (1979). NMR studies of laminaran: D. Gagnaire, *Org. Magn. Res.* **11,** 344 (1978); H. Friebolin *et al., ibid.* **12,** 216 (1979). *Review:* W. A. P. Black, E. T. Dewar in *Industrial Gums,* R. L. Whistler, Ed. (Academic Press, New York, 2nd ed., 1973) pp 137-145.

Water-insoluble laminaran, isolated from *L. cloustoni* Edmondst., *Laminariaceae,* is pptd spontaneously from the aq acid extract of the plant. Has lower degree of branching than the sol form. Typical analysis of the dry material: 92.5% polyglucose, 0.4% non-volatile matter; $[\alpha]_D^{16}$ −13.4° (c = 0.9). Amorphous triacetate, $(C_{12}H_{16}O_8)_n$, $[\alpha]_D^{16}$ −63.5° (c = 0.4 in chloroform).

Soluble form, isolated from *L. digitata,* is separated from the acidified extract only after addition of a precipitant such as ethanol. Typical analysis (on dry basis): 91.2% polyglucose, 1.0% non-volatile matter; $[\alpha]_D^{18}$ −11.9° (c = 2.1).

Sulfate, *laminaran hydrogen sulfate.* Laminaran can be sulfated to varying degrees. Highly sulfated products have anticoagulant properties comparable to heparin, while laminarans with few sulfate groups are antilipemic only: Besterman, Evans, *Brit. Med. J.* **1957, I,** 310.

5364. Laminin. Abundant structural component of the basal lamina; critical to the stability of the extracellular matrix and to the adhesion of cells to the basement membrane. Family of heterotrimeric glycoproteins composed of a heavy chain, designated α (also known as A) and 2 light chains, designated β (B1) and γ (B2), which are linked by disulfide bonds to form an asymetrical cross-shaped structure. Eight genetically distinct laminin subunits have been identified: α1, α2, α3, β1, β2, β3, γ1, and γ2. Seven different assembly forms (laminins-1 to -7) are known and appear to be tissue specific and developmentally reg Exhibits diverse biological activities. Influences adl growth, morphology and differentiation of a variety c via specific receptors including several of the integrir Isoln from murine Engelbreth-Holm-Swarm (EHS) t R. Timpl *et al., J. Biol. Chem.* **254,** 9933 (1979). Rev biological activities: H. K. Kleinman *et al., J. Cel chem.* **27,** 317-325 (1985); of role in neural developme Nurcombe, *Pharmacol. Ther.* **56,** 247 (1992). Tissue bution: E. Engvall *et al., Cell Regul.* **1,** 731 (1990). I of laminin binding proteins and receptors: R. P. Me *Ann. Rev. Cell Biol.* **7,** 71-91 (1991); and role in meta V. Castronovo, *Invas. Metast.* **13,** 1-30 (1993). Str and function of laminin isoforms: E. Engvall, *Kidn* **43,** 2-6 (1993); K. Tryggvason, *Curr. Opin. Cell Biol.* 5 882 (1993). Nomenclature: R. E. Burgeson *et al., J Biol.* **14,** 209 (1994). Review of structure: R. Timpl Brown, *ibid.* 275-281.

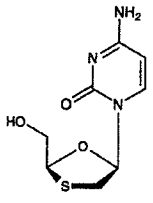
Laminin-1, *EHS-laminin.* Prototype laminin pro by murine EHS tumor. Contains α1 (also known as Ae), β1 (B1, B1e) and γ1 (B2, B2e) subunits.

Laminin-2, *merosin, laminin M.* Variant found in st muscle, placental trophoblast and Schwann cell bas membranes. Contains α2 (also known as M or Am), β γ1 subunits. Identification: I. Leivo, E. Engvall, *Proc Acad. Sci. USA* **85,** 1544 (1988); K. Ehrig *et al., ibi* 3264 (1990).

Laminin-3, *s-laminin, synaptic laminin.* Contains α (also known as s or B1s), and γ1 chains. Identificat neuromuscular junction: D. D. Hunter *et al., Natur* 229 (1989).

Laminin-5, *kallinin, nicein.* Contains α3, β3, and γ units. Isoln from human keratinocytes: P. Rousselle *J. Cell Biol.* **114,** 567 (1991).

5365. Lamivudine. *(2R-cis)-4-Amino-1-[2-(hyd methyl)-1,3-oxathiolan-5-yl]-2(1H)-pyrimidinone;* (- deoxy-3'-thiacytidine; (−)-1-[(2*R*,5*S*)-2-(hydroxyme 1,3-oxathiolan-5-yl]cystosine; 3'-thia-2',3'-dideoxycyt 3TC; (−)NGPB-21; (−)-BCH-189; GR-109714X; E $C_8H_{11}N_3O_3S$; mol wt 229.26. C 41.91%, H 4.84 18.33%, O 20.94%, S 13.99%. Reverse transcriptase i tor. Prepn: J. A. V. Coates *et al.,* **PCT Int.** pat. **17,159,** *C.A.* **117,** 111989 (1991). Synthesis of enantio J. W. Beach *et al., J. Org. Chem.* **57,** 2217 (1992); of enantiomer: D. C. Humber *et al., Tetrahedron Lette* 4625 (1992). Comparative *in vitro* anti-HIV activity: V. Coates *et al., Antimicrob. Ag. Chemother.* **36,** 733 (1 Clinical pharmacokinetics: R. van Leeuwen *et al., AI* 1471 (1992). HPLC determn in urine: D. M. Morri Selinger, *J. Pharmaceut. Biomed. Anal.* **12,** 255 (1994).



White solid from methanol/ethyl acetate. $[\alpha]_D^{21}$ − (c = 1.08 in methanol). Also reported as crystals boiling ethanol. mp 160-162°. $[\alpha]_D^{21}$ −135° (c = 0. methanol).

THERAP CAT: Antiviral.

5366. Lamoparan. Org-10172. Low molecular w heparinoid derived from porcine intestinal mucosa; mi of sulfated glycosaminoglycans with mean mol wt daltons. Prepn: A. L. M. Sanders *et al.,* **Eur. pat. 66,908;** *eidem,* **U.S. pat. 4,438,108** (1982, 1984 bot Akzo). Exhibits antithrombotic activity comparab standard heparin but with diminished hemorrhagic ef D. G. Meuleman *et al., Thromb. Res.* **27,** 353 (1982); H Cate *et al., ibid.* **38,** 211 (1985). Preliminary pharm kinetics and tissue distribution in humans: I. D. Bradb *et al., Brit. J. Clin. Pharmacol.* **23,** 667 (1987). Cli